## REMARKS

Claims 33-64 are in this application.

Claim 54 has been amended to delete the phrase "any one of the previous claims". Applicants preserve all rights to file one or more claims similar to claim 54 which depend from claims other than claim 33. Claims 33, 63 and 64 have been amended as discussed below.

Page 2 has been amended to delete the hyperlink.

The Examiner has rejected claims 33-45, 47, 56-61, 63 and 64 under 35 USC 112, first paragraph as not being enabled. Applicants respectfully traverse this rejection.

The Examiner takes the position that the specification does not provide enablement for "obtaining a probability of a hybridization signal". However, there is an extensive literature that deals with obtaining probabilities of a hybridization signal, so that methods of obtaining a probability of a hybridization signal are known to those versed in the art. An example of such knowledge is found in the attached article by Lipshutz, RJ, Likelihood DNA sequencing by Hybridization, J. Biomolecular . Structure. and Dynamics, , 11(3), pp 637-653, 1993. In the abstract of this publication it states that "...given a set of hybridizing probes, and the empirically derived rates of false positive and false negative hybridization, we can estimate the most likely DNA fragment to have produced the set of probes, and then estimate the probability that it generated the hybridization data". See also page 341 of this reference.

Therefore, it is respectfully requested that this rejection be withdrawn

The Examiner has rejected claims 33-45, 47, 56-61, 63 and 64 under 35 USC 112, second paragraph. Applicants respectfully traverse this rejection.

The Examiner alleges that step b in Claims 33, 63 and 64 is vague because the claims do not indicate "what the scoring algorithm is which calculates spectrum+sequence". Part b of Claims 33, 63 and 64 have been amended by including "the score being indicative of the candidate nucleotide sequence being a variant of H and furthermore being indicative of the probability that the candidate would give rise to the hybridization signal I(x)".

Support for this amendment is found *inter alia* on pages 5, 6-11 and 12 of the specification.

There is an extensive literature relating to this scoring procedure. Two publications where this is described are attached herewith:

S. Karlin, S. F. Altschul: "Applications and statistics for multiple high-scoring segments in molecular sequences" Proc. Natl. Acad. Sci. USA, vol. 90, pp. 5873-5877, 6/1993.

S. F. Altschul, T. L. Madden: "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs" Nucleic Acids Research, 1997, vol. 25, no. 17, pp. 3389-3402.

Accordingly it is respectfully requested that this rejection be withdrawn.

Applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted

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## MARKED-UP COPY

**In the Specification**

Page 2, paragraph 5, please replace as follows:

National Center for Biotechnology Information, 2000, A database of single nucleotide polymorphisms, World Wide Web address: ncbi.nlm.nih.gov/SNP./

**In the Claims**

Claim 33 (amended) A method for obtaining one or more candidate nucleotide sequences, the candidate nucleotide sequences being indicative of a sequence of a target polynucleotide molecule T, T producing a hybridization signal I $(\vec{x})$ upon incubating T with a polynucleotide $\vec{x}$ for each polynucleotide $\vec{x}$ in a set E of polynucleotides, the method comprising the steps of:

(a) for each polynucleotide $\vec{x}$ in the set E of polynucleotides, obtaining a probability $P_0(\vec{x})$ of the hybridization signal I $(\vec{x})$ when the sequence $\vec{x}$ is not complementary to a subsequence of T and a probability $P_1(\vec{x})$ of the hybridization signal when the sequence $\vec{x}$ is complementary to a subsequence of T; so as to obtain a probabilistic spectrum (PS) of T;

(b) assigning a score to each of a plurality of candidate nucleotide sequences, the score being obtained in a calculation using the probabilistic spectrum and at least one reference nucleotide sequence H, the score being indicative of the candidate nucleotide sequence being a variant of H and furthermore being indicative of the probability that the candidate would give rise to the hybridization signal I $(\vec{x})$; and

(c) selecting one or more candidate nucleotide sequences having an essentially maximal score.

Claim 54 (amended) The method according to [any one of the previous claims] claim 33 wherein the target comprises two or more polynucleotide molecules.

Claim 63 (amended) A program storage device readable by machine, tangibly embodying a program of instructions executable by the machine to perform method steps for obtaining a candidate nucleotide sequence, the candidate nucleotide sequence being indicative of a sequence of a target polynucleotide molecule T, T producing a hybridization signal I $(\vec{x})$ upon incubating T with a polynucleotide $\vec{x}$ for each polynucleotide $\vec{x}$ in a set E of polynucleotides, the method comprising the steps of:

(a) for each polynucleotide $\vec{x}$ in the set E of polynucleotides, obtaining a probability $P_0(\vec{x})$ of $I(\vec{x})$ when the sequence $\vec{x}$ is not complementary to a subsequence of T and a probability $P_1(\vec{x})$ of $I(\vec{x})$ when the sequence $\vec{x}$ is complementary to a subsequence of T; so as to obtain a probabilistic spectrum (PS) of T;

(b) assigning a score to each of a plurality of candidate nucleotide sequences, the score being obtained in a calculation using the probabilistic spectrum and upon at least one reference nucleotide sequence H, the score being indicative of the candidate nucleotide sequence being a variant of H and furthermore being indicative of the probability that the candidate would give rise to the hybridization signal $I(\vec{x})$; and

(c) selecting one or more candidate nucleotide sequences having an essentially maximal score.

Claim 64 (amended) A computer program product comprising a computer useable

medium having computer readable program code embodied therein for obtaining a candidate nucleotide sequence, the candidate nucleotide sequence being indicative of a sequence of a target polynucleotide molecule T, T producing a

hybridization signal I $(\vec{x})$ upon incubating T with a polynucleotide $\vec{x}$ for each polynucleotide $\vec{x}$ in a set E of polynucleotides, the computer program product comprising:

(a) for each polynucleotide $\vec{x}$ in the set E of polynucleotides, computer readable program code for causing the computer to obtain a probability $P_0(\vec{x})$ of $I(\vec{x})$ the sequence $\vec{x}$ is not

complementary to a subsequence of T and a probability $P_1(\vec{x})$ of $I(\vec{x})$ when the sequence $\vec{x}$ is complementary to a subsequence of T;

(b) computer readable program code for causing the computer to assign a score to each of a plurality of candidate nucleotide sequences, the score obtained in a calculation using the probabilistic spectrum and at least one reference nucleotide sequence H, the score being indicative of the candidate nucleotide sequence being a variant of H and furthermore being indicative of the probability that the candidate would give rise to the hybridization signal $I(\vec{x})$; and

(c) computer readable program code for causing the computer to select a candidate nucleotide sequence having an essentially maximal score.